In-silico Development- and Clinical-Trial-Platform for Testing in-situ Tissue Engineered Heart Valves – SimInSitu

PI Caterina Gandolfo, MD, PhD

Ente Finanziatore: Commissione Europea

Bando: H2020-SC1-DTH-2020-1 Digital transformation in Health and Care - Topic SC1-DTH-06-2020 Accelerating the uptake of computer simulations for testing medicines and medical devices

Tipologia di azione: RIA (Research and Innovation action)

Costo complessivo del progetto: euro 5.410.692,50

Contributo CE: euro 5.410.692,50

Budget ISMETT: euro 187.500

Coordinatore: 4RealSim Services B.V. (NL)

Partners: ISMETT, Università degli Studi di Palermo (IT), Association Pour La Recherche Et Le Developpement Des Methodes Et Processus Industriels (FR), LEARTIKER, SCOOP (ES), XELTIS BV (NL), CAPVIDIA (BE), Technische Universitaet Graz (AT), Katholieke Universiteit Leuven (BE)

Durata: 48 mesi Progetto approvato e in fase di definizione del Grant Agreement

Background

Currently the standard treatment of diseased valves exhibiting functional impairment with clinical consequences is the replacement of the valve with either a surgical valve or a transcatheter valve. Most of the commercially available transcatheter devices are bio-prosthetic, which typically comprise leaflets and other components manufactured from processed animal tissue. Due to the harsh biomechanical and hemodynamic environment, especially in the left heart side, and the lack suitable synthetic material capable to withstand this load, bioprosthetic heart valves suffer predominantly from age related structural deterioration1, which limits the realistic life-span of these devices to 10-15 years. As the age of patients that are treated with bio-prosthetic heart valves is decreasing, this limited life-span causes an increasing need for revision interventions.

Tissue engineered heart valves are considered a smart solution for the problems mentioned above, by creating a living autologous device that has the capability to remodel and grow during the patient's lifetime and do not trigger an immune response.

Innovazione e impatto

SimInSitu project will investigate the next generation heart valves fabricated with biodegradable synthetic materials to eliminate the need for animal models and thus reduce the cost related to device fabrication. Synthetic electrospun-based Xeltis devices have demonstrated to be safe in clinical applications, suggesting a new paradigm for heart valve technology not based on animal tissue materials. In the SimInSitu project, the efficacy of synthetic valve leaflets materials will be investigated by in-silico modelling to provide a reliable approach to design the next generation of heart valves and thus offer a numerical framework to test the efficacy of synthetic valve materials

even to other heart valve manufactures and research group. The SimInSitu project will therefore relax restrictions imposed by cost and ethical considerations.

Obiettivi dello progetto

SimInSitu is aiming to develop a sophisticated in-silico method to predict the short- and long-term behavior of in-situ tissue engineered heart valves by combing advanced tissue remodeling algorithms with a personalized virtual heart modelling approach. The method will be specifically developed to predict the complex transformation process of biodegradable heart valves from the initially synthetic scaffold into a fully remodeled & functional valve. This transformation process, named ETR for Endogenous Tissue Restoration, is the core technology for a new generation of very promising biodegradable vascular device currently developed by Xeltis. ETR makes the use of animal derived tissue, which is used in the majority of commercially available bioprosthetic heart valves, obsolete and avoids thereby durability related issues and potentially minimized the need for reoperations. Though, significant progress was made during the past years in developing ERT based devices, it remains very challenging, costly, time-consuming, and rich with obstacles. New knowledge can only be generated through a tedious trial & error process (requiring preclinical and clinical studies), since the restorative process cannot be replicated in an in-vitro environment. Advanced Computer Modelling & Simulation technologies have the potential to overcome this limitation by allowing to test new designs, modified scaffold compositions, or other applications in a virtual patient-specific environment – in-silico. SimInSitu will not only develop such a computer model, but will also verify and validate it thoroughly by making use of the extensive in-vitro and in-vivo data available and where necessary will generate new data to support the credibility of this in-silico method. The availability of this computer model could contribute significantly to an acceleration of especially the ETR-device development and accelerate their translation into the clinic and market.

Pubblicazioni/Risultati raggiunti